being reported in greater detail elsewhere. The data already presented, however, serve to stress the necessity of avoiding the mixing of clotting reagents derived from different species. This is particularly applicable to thromboplastins and antithromboplastins, a precaution that has been stressed by us[7] and others.[13]

No direct correlation seems to exist between the effectiveness of heparin and the lipid inhibitor as tested *in vivo* and *in vitro*. While heparin is the stronger anticoagulant, the fact that it is rapidly excreted or inactivated *in vivo* has seriously limited its clinical usefulness. The longer duration of the effect of an intravenous injection of the lipid anticoagulant when compared with that of heparin seems to make the lipid more suitable in the anticoagulant therapy of thromboembolic disease.[14]

Summary. A heat labile lipid inhibitor of blood coagulation has been extracted from brain tissue, differing in potency and other respects from similar known anticoagulants. It has a pronounced antithromboplastic activity especially against homologous brain extracts in homologous plasma. Though the anticoagulant power of this lipid antithromboplastin *in vitro* is still less than that of heparin, it has a more lasting effect when injected intravenously than a solution of heparin of equivalent potency.

13 Fantl, P., and Nance, M. A., *Med. J. Australia*, 1946, **2**, 125.

14 Tocantins, L. M., Carroll, R. T., and McBride, T. G., *Fed. Proc.*, 1948, **7**, 125.

16409

Blood Volume and Sympathectomy in Hypertension.

W. D. DAVIS, JR., AND H. S. MAYERSON.

From the Departments of Medicine and Physiology, Tulane University School of Medicine, and the Alton Ochsner Medical Foundation, New Orleans.

It has been observed that in hypertensive patients following sympathectomy there frequently is a return of blood pressure to the preoperative level after a brief period of relative hypotension. Since blood volume is an important factor in maintenance of the blood pressure level, it seemed advisable to investigate the possible changes in blood volume consequent to the postulated enlargement of the vascular bed produced by sympathectomy and to correlate these changes with those in the blood presure. Our results indicate that there are no consistent changes in total blood volume or in plasma volume during periods as long as 18 months after operation. Immediate postoperative reduction in red cell mass with concomitant increase in plasma volume occurred frequently and persisted in many cases. The postoperative prognosis in patients with low red cell mass preoperatively seemed to be poor.

Adequate postoperative determinations were available for 20 patients, 11 of whom were women and 9 men, ranging in age from 22 to 50 years. Follow-up observations ranged from 3 to 18 months. Thoracolumbar sympathectomy was done in all cases except one in which the transthoracic approach was used. Plasma volumes were measured photocolorimetrically with the T-1824 dye according to the procedures outlined by Gregersen.[1] Hematocrit readings were obtained by the Wintrobe method and these values were employed to calculate whole blood and red cell volumes. Standard values of 45 cc/kg were used for the plasma volumes of men, 40 cc/kg for women and 40 and 35 cc/kg for red cell volumes in men and women, respectively.

1 Gregersen, M. I., *J. Lab. and Clin. Med.*, 1944, **29**, 1266.

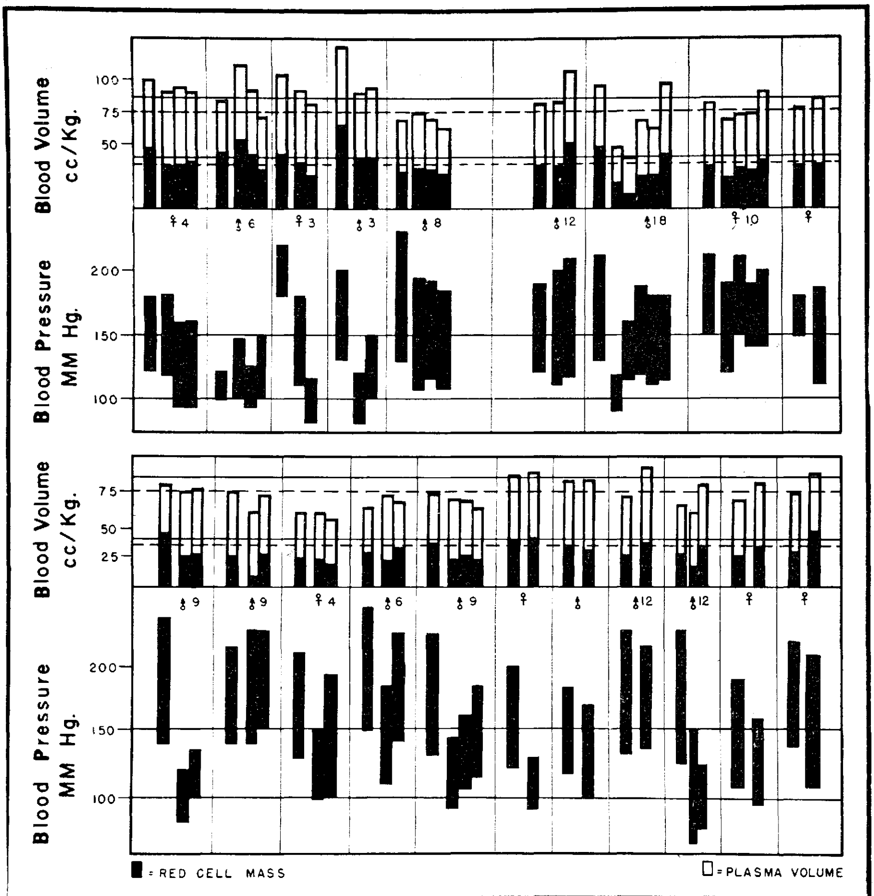

FIG. 1.

Relationship of plasma, red cell, and total blood volume to blood pressure. Each group of bars represents one patient and the first bar of each group represents the preoperative level. The shaded part of the blood volume bar represents red cell volume and the unshaded part is plasma volume. The small figures denote the duration of follow-up in months.

No consistent variation in blood volume from "normal" levels was observed preoperatively.[2,3] The results are shown in Fig. 1. In the first 4 patients there was close agreement between the post-operative drop in blood pressure and the changes in blood volume even for each individual determination. This would suggest that the blood volume change had a significant effect on the blood pressure or that the vascular tree was somewhat underfilled as a result of post-operative vasodilation.

In the next patient there was close agreement between the blood volume and blood pressure as the latter rose postoperatively and in the next case there was similar postoperative agreement until 18 months after operation when the blood volume returned to the preoperative level while the blood pressure was still significantly reduced. In the subsequent cases there was a sharp drop in blood pressure with little or no alteration in blood volume, as well as changes in blood volume with no change in blood pressure. Thus,

[2] Harris, A. W., and Gibson, J. G., Jr., *J. Clin. Invest.*, 1939, **18**, 527.

[3] Rowntree, L. G., and Brown, G. E., *The Volume of the Blood and Plasma in Health and Disease*, Philadelphia, W. B. Saunders & Co., 1929, p. 158.

the absence of obligate relationship is emphasized. There was also no correlation between postoperative blood volume and postural changes in blood pressure. These results are in agreement with those of Freis and Smithwick,[4] who studied 10 patients for 6 months postoperatively.

Immediately following operation there was a significant decrease in total red cell volume in the majority of patients (Fig. 2.). In many of these, return to standard levels was delayed for considerable periods postoperatively (Fig. 3). When the patients were grouped with regard to the manometric and symptomatic response to operation (Fig. 4), it was seen that the 5 patients who had exceptionally poor postoperative results all had low circulating red cell masses before operation whereas the 5 who had good results exhibited normal, or in 3 cases, elevated red cell masses preoperatively. There was a general tendency for patients with long standing or severe vascular disease to have low red cell masses and total blood volumes.[5]

The postoperative changes fall into several interesting groups. There was a general tendency for the red cell mass to drop immediately after the operation with a concomitant increase in plasma volume. These

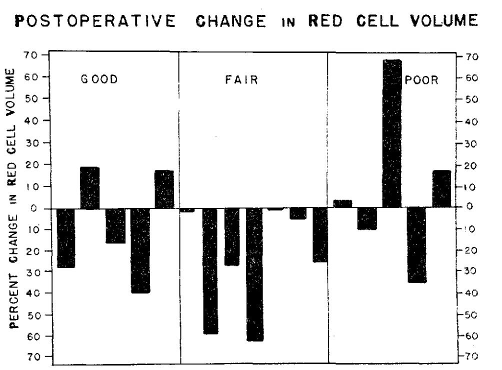

FIG. 2.
Changes in red cell volume approximately 2 weeks after sympathectomy. In this and in succeeding figures the patients are grouped with regard to symptomatic and manometric responses. Each bar represents one patient.

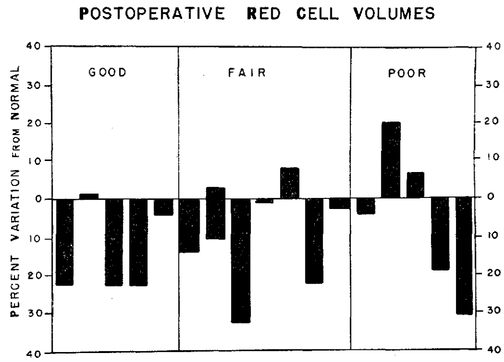

FIG. 3.
Red cell volumes at conclusion of experiments. See Fig. 1 for duration of follow-up periods.

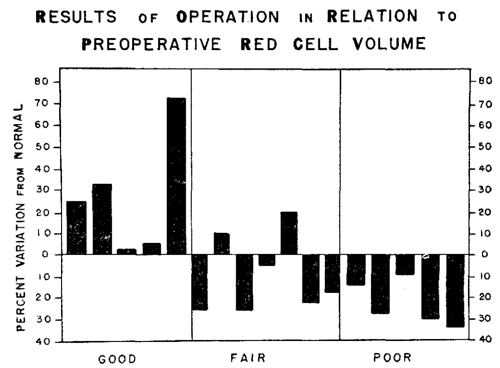

FIG. 4.
Relationship of preoperative red cell volume to operative response.

changes cannot be ascribed to bed rest alone, since prolonged bed rest results primarily in a decrease in plasma volume.[6] We believe that the decrease in red cell volume is a nonspecific effect related to postoperative blood loss;[4] this would suggest that more adequate blood replacement during operation might be indicated. The persistent low red cell levels are more difficult to explain. Schafer[7] reported a decrease in red cell mass in sympathectomized hypertensive dogs and in one patient with polycythemia vera and suggested that sympathectomy resulted in improved blood flow to the bone marrow and a consequent decrease in erythropoetic stimulus. Freis and Smithwick[4] also noted a tendency

---

4 Freis, E. D., and Smithwick, R. H., *Am. J. M. Sc.*, 1947, **214**, 363.

5 Clark, J. H., Nelson, W., Lyons, C., Mayerson, H. S., and DeCamp, P., *Ann. Surg.*, 1947, **125**, 618.

6 Taylor, H. L., Erickson, L., Henschel, A., and Keys, B., *Am. J. Physiol.*, 1945, **144**, 227.

7 Schafer, P. W., *Ann. Surg.*, 1945, **122**, 1098.

for hematocrit values to remain low after sympathectomy but suggested that the change might be more apparent than real. They believe that sympathectomy, by altering the caliber of the smaller vessels, may cause redistribution of the red cell mass in the vascular system. This in turn would change the cell-plasma ratio in the larger vessels from which sampling is accomplished. Although this possibility cannot be excluded, it can hardly be of the magnitude and persistence required to explain our observations. In addition, any significant changes resulting from sympathectomy involve arterioles rather than capillaries and should not necessarily result in the shifting of large portions of the blood volume. The absence of any significant increase in blood volume after sympathectomy raises the question as to whether any widespread dilatation has actually occurred. A similar pronounced reduction in hematocrit was observed by Green[8] after surgical removal of a pheochromocytoma. The explanation of these observations is as yet obscure.

Although our series is admittedly small, it seems probable that patients with low red cell masses preoperatively can expect little from sympathectomy whereas if the red cell mass is elevated the prognosis is considerably better. Whether this is simply another way of saying that patients operated on early in the course of the disease do better postoperatively cannot be determined from these data.

Summary. Blood volume studies on 20 patients with hypertensive vascular disease before and after sympathectomy revealed no consistent long-term postoperative changes other than immediate decrease in the red cell mass with tendency toward delayed recovery. There was no consistent deviation from "normal" in the preoperative determination. Patients with low red cell masses preoperatively showed poor postoperative response and there was a general tendency for patients with long-term vascular disease to have low blood volume.

8 Green, D. M., *J. A. M. A.*, 1946, **131**, 1260.

16410 P

Production of Alloxan Diabetes in the Dog.

L. J. MANHOFF, JR., AND A. WILLIAM DELOACH. (Introduced by Edgar J. Poth.)
From the Surgical Research Laboratory, University of Texas Medical Branch, Galveston, Tex.

The discovery that a diabetic state could be induced in experimental animals by a single injection of alloxan opened a new field for the investigation of problems relating to the control of sugar metabolism. This technique has been applied and found successful in most of the ordinary species of laboratory animals. However, the results are not nearly so satisfactory in one of the more valuable experimental animals, the dog. Ordinarily, a satisfactory diabetic dog is obtained in only one out of 7 or 8 attempts. Doses of alloxan greater than 100 mg per kilo are frequently fatal, and smaller doses usually do not produce an appreciable and sustained elevation of the blood sugar. Failures in these larger laboratory animals is expensive and time consuming and makes a more effective method desirable.

The alloxan in varying dosages was injected directly into the abdominal aorta, and the hepatic, gastro-duodenal, and pancreatic arteries in an attempt to obtain a higher concentration of the drug in the pancreas with a smaller amount of the drug in the general circulation, thereby avoiding toxic effects on other organs. These attempts failed: only one in 8 dogs developed a moderate hyperglycemia and this effect did not persist longer than 2 weeks.

Kass and Waisbren[1] increased the per-

1 Kass, E. H., and Waisbren, B. A., PROC. SOC. EXP. BIOL. AND MED., 1945, **60**, 303.